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13. ABSTRACT *(Maximum 200*
The Robert H. Lurie Cancer Center at Northwestern University is an NCI-funded comprehensive cancer center. The Cancer Center has made significant advances in developing a premier breast cancer program. In September, 1994, the Cancer Center received a four year award from the US ARMY for comprehensive training of graduate students conducting breast cancer relevant research entitled, "Molecular Biology of Breast Neoplasia". This program exposes four students per year to the latest developments in breast cancer biology and treatment. Students receive laboratory training with senior basic science faculty and clinical investigators provide a translational link. In June 1995, the Cancer Center applied for and received a supplement to the Training Grant through the National Action Plan on Breast Cancer, Public Health Services Office on Women's Health. The award funds one postdoctoral position per year for a period of three years. Members of the program participate in a weekly Journal Club and a monthly breast cancer research meeting to augment their research training. The publication records of the trainees is indicative of the success of the Training Grant. The instruction received by the trainees puts them in an ideal position to contribute to advancements in the treatment and prevention of breast cancer.

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FOREWORD

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PI - Signature

9/24/97
Date

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Introduction

The Robert H. Lurie Cancer Center has been funded by a cancer center support grant from the National Cancer Institute since 1993. The mission of the Cancer Center is to promote clinical and laboratory research at the Northwestern Medical School and its five affiliated hospitals and in the basic science departments located on the Evanston Campus. The Cancer Center strives for excellence in cancer research, prevention, diagnosis, treatment and rehabilitation, as well as in education of scientists, health professionals and the community. The Cancer Center is dedicated to encourage the rapid application of new technology to patient care. The affiliated hospitals of Northwestern treat a total of more than 5,000 cancer patients per year.

Since 1993, the Lurie Cancer Center has made significant advances in developing a premier breast cancer program at Northwestern University. In October, 1993, the Cancer Center recruited V. Craig Jordan, Ph.D., D.Sc. to direct the breast cancer laboratory research program and Monica Morrow to direct the clinical breast cancer research program and the Lynn Sage Comprehensive Breast Center at Northwestern. Dr. Jordan is an internationally recognized leader in breast cancer research. His most important contribution to the field has been in the research and development of the antiestrogen tamoxifen, an important drug used in the treatment of breast cancer. In September 1994, the Cancer Center successfully competed for a grant from the NCI to establish a breast cancer program (NCI 1P20 CA65764). The co-principal investigators of this grant were Drs. Jordan and Morrow. Other breast cancer focused research awards include 6 grants from the US Army Breast Cancer Research Program, interactive RO1's from the NCI focused on hormonal and nutritional aspects in breast cancer prevention, an R21 translational research grant in angiogenesis, an RO3 grant to establish the Y-ME support group on the Internet, and Illinois Department of Public Health Cancer Research Grants on breast cancer prevention, early detection and translational research. In August, 1996, the Cancer Center was selected as one of three institutions in the US to receive a four year breast cancer center grant from the US Army (DAMD17-96-2-6013). The title of the grant is "Increasing Access to Modern Multidisciplinary Breast Cancer Care". Principal Investigator is Monica Morrow, M.D.. The award provides funds for eight research projects that address access to breast cancer care by minority women, education of minority women, dietary intervention to reduce cancer risk, methods to increase minority participation in clinical trials and cost effectiveness of new technologies.

Body

In September 1994, the Cancer Center also received a four year award from the US Army for training of graduate students conducting breast cancer relevant research entitled, "Molecular Biology of Neoplasia". This program provides students with comprehensive training in breast cancer biology, utilizing the powerful tools of molecular biology, genetics and biochemistry to unravel the complex mechanisms of breast neoplasia. The program enables four students per year to be exposed to senior basic science faculty with research relevant to breast cancer research and to clinical investigators who provide a translational link.

In June, 1995, the Cancer Center applied for and received a supplement to the Training Grant through the National Action Plan on Breast Cancer (NAPBC), Public Health Services Office on

Women's Health. The award was made to the Cancer Center through the Department of Defense. The Center received funds for three postdoctoral positions, one per year for a period of three years.

Each year the Cancer Center solicits applications from faculty in the Breast Cancer Program nominating students. Typically, 10 applications are received each year for the predoctoral training and three applications for the single postdoctoral position. The Training Grant advisory committee is responsible for the selection of students. Committee members include: V. Craig Jordan, Ph.D., Steven Rosen, M.D., Director, Lurie Cancer Center, Robin Leikin, Ph.D., Training Grant Administrator; Kathleen Rundell, Ph.D., Professor, Microbiology-Immunology; Janardan Reddy, M.D., Professor, Pathology; and Daniel Linzer, Ph.D., Associate Professor, Biochemistry, Molecular Biology and Cell Biology. Students are selected based upon their academic credentials, the relevance of their research projects to breast cancer and their potential as future academicians in breast cancer research.

Multidisciplinary Approach

The following predoctoral and postdoctoral students have been allocated funds through the Molecular Biology of Breast Neoplasia Training Grant:

Year 1:

Name	Principal Investigator	Department
S-J Teng	Daniel Linzer, Ph.D.	BMBCB
Sameer Mathur	Richard Morimoto, Ph.D.	BMBCB
M. Shanmugam	Mary Hunzicker-Dunn, Ph.D.	Cell & Mol Biology
Julie McLachlan	Ouahid Bakouche, Ph.D.	Molec Pharm & Biological Chem

BMBCB Biochemistry, Molecular Biology and Cell Biology

Year 2

Name	Principal Investigator	Department
Ann Buchmann	Bayar Thimmapaya, Ph.D.	Micro-Immuno
Stephanie Hsu	Noel Bouck, Ph.D.	Micro-Immuno
Todd McAdams	Terry Papoutsakis, Ph.D. William Miller, Ph.D.	Chem Engineering
M. Shanmugam	Mary Hunzicker-Dunn, Ph.D.	Cell & Molec Biol

Zehan Chen, Ph.D.	V. Craig Jordan, Ph.D.	Cancer Center

Year 3

Student	Principal Investigator	Department
Ann Buchmann	Bayar Thimmapaya, Ph.D.	Micro-Immuno
Kristi Miller	Sigmund Weitzman, M.D.	Medicine
Jennifer MacGregor	V. Craig Jordan, Ph.D.	Cancer Center
Jennifer Sanders	Paula Stern, Ph.D.	Molec Pharm & Biol Chem
Sonia Cerda, Ph.D.	Sigmund Weitzman, Ph.D.	Medicine

Year 4

Student	Principal Investigator	Department
Jennifer MacGregor	Craig Jordan	Cancer Center
Kristi Miller	Sigmund Weitzman	Medicine, Heme/Onc
Mairin Anderson	Brian Hoffman	Chemistry
Ken Geles	Stephen Adam	Cell & Molec Biology
Larissa Wenning, Ph.D.	Bill Miller/ Terry Papoutsakis	Chem Engineering

S-J Teng

Studies of the Expression of Prolactin Receptors and the Effects of Targeted Disruption of this Receptor Gene During Mouse Embryogenesis

Mr. Teng has studied the developmental pattern of prolactin receptor expression in the mouse. Mice synthesize at least four forms of the receptor. He has found maximum levels of receptor mRNA in mouse embryos at days 8 and 18, but levels decreased between these days to a minimum at day 14, In contrast, levels of placental prolactin receptor mRNA remained constant throughout gestation. On embryonic day 16, the mRNA encoding the long form of prolactin receptor is more abundant in the fetal liver than any of the short receptor form mRNAs, but by day 18 a switch occurs and the mRNA encoding one of the short receptor forms becomes the predominant receptor mRNA in the liver. Expression of prolactin receptor mRNA and protein is abundant throughout the fetus, with particularly high levels in the bone and cartilagenous structures, brain, thymus, pituitary, tongue, and skeletal muscle. The pattern of expression of prolactin receptor in the fetal mouse suggests an important role for the placental lactogens, the major ligands for fetal prolactin receptors in fetal growth and development. Mr. Teng has just published his research in a manuscript entitled, " Prolactin

Receptor Expression in the Developing Mouse Embryo" to the journal Molecular Reproduction and Development. Since prolactin is one of the primary regulators of mammary gland development and function, an understanding of the mechanisms of action of the receptors for this hormone is central to understanding the abnormal mammary gland in breast cancer.

Sameer Mathur

Characterization of the Chromosomal 6 HSP70 Locus in Y79 Retinoblastoma Cells

Cellular stresses are associated with activation of the heat shock gene transcription. There are four known heat shock transcription factors, HSF1-4. Mr. Mathur is studying the signal transduction pathway for the heat shock protein transcription factor HSF2. HSF2 is activated in response to hemin, an inhibitor of proteasome activity. Mr. Mathur tested other inhibitors of proteasome activity for their ability to activate HSF2. Gel mobility shift assays were carried out. Antibodies to HSF2 demonstrated that the DNA binding activity induced by the various proteasome inhibitors was HSF2. Furthermore, HSF2 activation resulted in induction of heat shock protein expression. The induction of heat shock proteins and proteasome activity suggests a role for the heat shock proteins in chaperoning polyubiquitinated proteins. In order to test this hypothesis, immunoprecipitations of hsp70 were performed and the complexes examined for the presence of polyubiquitinated proteins. The results reveal such an interaction between hsp70 and polyubiquitinated proteins. HSF2 is a key regulatory transcription factor for the molecules HSP70 and HSP90, both of which are important regulatory proteins for estrogen, progesterone and glucocorticoid receptors. This has direct relevance to breast cancer because heat shock proteins may regulate the estrogen receptor.

Malathy Shanmugam

Characterization of the Protein Kinase C Delta Isoform in Human Breast Cancer Cell Lines

Ms. Shanmugam has demonstrated that protein kinase delta (PKC δ) is the predominant isoform of PKC in estrogen responsive MCF-7 cells and is absent from estrogen unresponsive MDA-MB human breast cancer cells. She has shown that estrogen's enhancement of proliferation in MCF-7 cells is directly linked to the down regulation of PKC δ mRNA and protein. MDA-MB have reduced levels of PKC δ which may explain in part their more aggressive phenotype. Growth inhibition of MCF-7 estrogen positive cells using phorbol ester leads to PKC δ activation and induction of the cyclin-dependent kinase inhibitor p21Wafl/Cipl. The results suggest that activated PKC delta may signal to initiate/maintain the growth arrest of breast cancer cells. Ms. Shanmugam has recently published her results in the Journal of Biological Chemistry. She completed her Ph.D. training in June, 1997 and is pursuing a postdoctoral position in the field of breast cancer research.

Julie McLachlan

The Effect of Age on the Activation and Cytotoxicity of Human Monocytes

Monocytes isolated from aged individuals (aged monocytes) are greatly deficient in their cytotoxic and tumoricidal abilities when compared to monocytes isolated from young individuals (young monocytes). Ms. McLachlan examined the biochemical, molecular and signal transduction differences between young and aged monocytes by studying the effects of

the adrenal androgen dehydroepiandrosterone (DHEA) in immunity. DHEA is the precursor of androgens and estrogens. DHEA and LPS (lipopolysaccharide) at 0.2 ng/ml displayed a synergistic effect on monocyte cytotoxicity against cancerous cell lines, IL-1 secretion, reactive nitrogen intermediate release, complement receptor-1 cell-surface protein, and TNF- α protein to levels comparable with levels obtained using LPS at 1.0 ug/ml. Monocytes stimulated with DHEA alone or with LPS at low concentrations did not display markers of cytotoxicity. DHEA receptor could be measured in monocytes, suggesting that DHEA effects on LPS-stimulated monocytes are mediated through a receptor-dependent process. Monocytes play a prominent role in host defense against breast cancer through a surveillance mechanism, so breast cancer in the elderly may correlate with a decrease in the efficiency of monocytes to develop a cytotoxic phenotype in elderly.

Ann Buchmann

Regulation of Gene Expression by pRb using a Novel Approach

Ms. Buchmann is studying the genes that are transcriptionally controlled by retinoblastoma protein. Specifically, the retinoblastoma tumor suppressor gene product (pRb) controls cell cycle progression from G1 into S. Mutation of pRb or deletion of the Rb gene has been seen in 20-30% of breast cancers. Reintroduction of normal Rb gene into breast cancer cells that have lost Rb function causes the cells to lose their ability to form tumors in nude mice, indicating that loss of pRb contributes to the tumorigenicity of these cells. pRb functions by binding to and regulating the activities of several transcription factors, suggesting that pRb controls the transcription of specific genes. Ms. Buchmann has used adenovirus vectors to overexpress pRb, in the cell lines SAOS (human osteosarcoma) and MCF-10 (breast cancer) in G1 phase of the cell cycle. RNase protection assays indicate that pRb is involved in the transcriptional downregulation of E2F-1, E2F-2, DHFR (dihydrofolate reductase), thymidine kinase, c-myc, PCNA, p107, and cyclin inhibitor p21. pRb has no effect on the transcription of E2F-3, E2F-5, DP-1, DP-2 or cyclin inhibitor p16. These results suggest that pRb controls the transcription of genes involved in G1 to S phase progression. This research complements the research of Dr. Thimmapaya who is developing viral vectors with breast cell specific promoters to deliver suicide genes such as thymidine kinase and cytidine deaminase into breast tissues.

Stephanie Hsu

Tumor Suppressor Gene Control of Angiogenesis in Glioblastoma Multiforme Cell Lines

Ms. Hsu is looking at the role of tumor suppressors and angiogenesis in human glioblastoma cell lines. The growth of glioblastoma tumors depends on the loss of tumor suppressor genes on chromosome 10 and angiogenesis. When wild type chromosome 10 is transferred into human glioblastoma cell lines, tumor growth is inhibited. This inhibition is due to the loss of angiogenic activity through increased secretion of an inhibitor of angiogenesis, thrombospondin-1. Anti-thrombospondin antibodies completely reverse this inhibition. This work has been extended to patient samples. Normal brain and low grade astrocytomas known to retain chromosome 10 stain strongly for thrombospondin, but 12/13 glioblastomas, which have no chromosome 10, do not stain for thrombospondin. This study suggests that loss of tumor suppressor genes on chromosome 10 contributes to the aggressive phenotype of glioblastomas, in part by releasing constraints on angiogenesis that are normally maintained

by thrombospondin. This research is directly related to Dr. Bouck's other research endeavors in breast cancer, where angiogenesis is known to play an important role in the progression of disease. Dr. Bouck has shown that thrombospondin is produced by normal breast epithelial cells, but is lost in breast tumors. Ms. Hsu recently was awarded the Ph.D. degree. Upon completion of her medical training, she will pursue a career in academic research.

Todd McAdams
Improved Substrates and Culture Conditions for the Ex Vivo Expansion of Primitive Hematopoietic Cells
Mr. McAdams is examining optimization of culture pH for improving the expansion of peripheral blood stem cells from breast cancer patients who are undergoing peripheral blood stem cell (PBSC) transplantation. PBSC has the advantage over bone marrow in terms of fewer contaminating tumor cells and for increasing the rate of engraftment/hematopoietic recovery following transplantation. However, PBSC contain tumor cells. Purging methods eliminate rapidly dividing tumor cells, but also eliminate the rapidly dividing committed hematopoietic progenitors. One solution is to use ex vivo methods to expand the PBSC following purging to eliminate tumor cells. Specifically, Mr. McAdams is studying peripheral blood CD34+ cells cultured under a range of pH values from 7.15 to 7.6. Cultures at high pH contained greater numbers of hemoglobin positive and band 3 positive cells, and acquired erythroid differentiation markers sooner than standard and low pH cultures. Flow cytometry using CD71 and CD45RA antigens also indicated that differentiation proceeded faster at high pH and was blocked at an intermediate stage by low pH. Morphological studies confirmed that high pH cultures shifted towards late stage erythroid compartments as compared to low and standard pH cultures. These results have important applications for the ex vivo expansion of erythroid progenitors used in peripheral blood stem cell transplantation.

Malathy Shanmugam
Ms. Shanmugam was funded for a second year for her research of PKC delta isoform in breast cancer cell lines (see above).

Zehan Chen, Ph.D.
Identification of Genes Related to Estrogen Receptor Independent Proliferation Pathways
Dr. Chen is studying the role of methylation in down regulation of estrogen receptors (ER) in breast cancer cells, testing the hypothesis that methylation of the CpG island is the fundamental mechanism responsible for the loss of ER expression in breast cancer cells. The model for these studies is a cell line C4:2 derived in the Jordan laboratory from an ER positive breast cancer cell line grown long term in estrogen-free medium. The C4:2 has irreversibly lost expression of ER and is no longer hormone responsive. Dr. Chen shows that the ER CpG island in the C4:2 cells remains unmethylated. The loss of the ER in the cell line must be due to other mechanisms rather than methylation. His studies due not rule out that methylation may be an event that occurs subsequent to loss of the ER expression. Dr. Chen recently completed his postdoctoral training to accept a position working in breast cancer research for a pharmaceutical company.

Ann Buchmann
Ms. Buchmann was funded for a second year for her research on pRb. (see above)

Kristi Miller
The Role of p300 in Breast Morphogenesis
Ms. Miller is studying the role of the transcriptional coactivator p300 in breast cell morphogenesis in vitro. An understanding of the process normal breast cells undertake in morphogenesis should be valuable in understanding breast cancer progression. Since the ability to form structures is lost early in malignant cells, factors controlling morphogenesis may help to explain the mechanisms involved in malignancy. p300 is a nuclear phosphoprotein involved in differentiation. Phosphorylation of p300 is correlated with activation of c-jun transcription. Kristi is attempting to identify regions on the p300 molecule that are linked to breast cell morphogenesis. She will generate mutant vectors for these studies. Kristi has demonstrated that expression of a mutant p300 protein completely blocks duct formation in vitro.

Jennifer MacGregor
Re-introduction of the Estrogen Receptor (ER) into T47D Breast Cancer Cells to Re-establish the Hormone Responsive Phenotype
Ms. MacGregor is studying the differential effects of estrogen and antiestrogens and their effect on growth and gene regulation in T47:A18 (ER positive) and T47D:C4:2 (ER negative) breast cancer cell lines. These subclones were derived in Dr. Jordan's laboratory from the parent T47D human breast cancer cell line. Ms. MacGregor will determine expression levels and mutational status of the p53 tumor suppressor gene and BRCA1 breast cancer gene in the T47:A18 and T47D:C4:2 cell lines. She will also transiently and stably transfect ER cDNA into the each of the subclones and look at estrogen and antiestrogen responsiveness. Her results should provide important information about the role of the ER in the progression from hormone dependent to hormone independent growth.

Jennifer Sanders
Role of Protein Kinase C (PKC) Isozymes in the Anti-osteoporotic Effects of Estrogen and Antiestrogens
Ms Sanders is studying the effects of estrogen and tamoxifen on bone. Experimental and clinical studies suggest that tamoxifen acts like estrogen on bone, promoting the conservation of bone tissue. Specifically, Ms. Sanders is examining the PKC signal transduction pathway in osteoblasts. PKC isozyme expression was measured in rat osteosarcoma cells treated with estrogen or tamoxifen by Western immunoblotting. Only 3 or 7 day hormone treatment modulated isozyme expression. The observed effect was an increase in PKC- β1 expression. This isozyme may play a role in the bone-preserving effects of estrogenic agents. Ms. Sanders has already published some of her research in the Journal of Bone and Mineral Research and her most recent work was published in The Pharmacologist and presented at the Pharmacology '97 Meeting. Ms. Sanders was recently awarded her Ph.D. degree. She is

currently a postdoctoral research associate carrying out research in women's health at Brigham and Women's Hospital in Boston, MA.

Sonia Cerda, Ph.D.
Oxidative DNA Damage Repair in Breast Cancer
Dr. Cerda is studying the role of the DNA repair gene, alkyl-N-purine-DNA glycosylase (ANPG), in a variety of human breast cancer cell lines and tissues. MDA-MB 231, MCF 7 and T47D breast cancer cell lines exhibited 3,10 and 14 times higher levels of ANPG mRNA than normal breast epithelium. Analysis of DNA from the cell lines by Southern blot indicated no ANPG amplification. Immunohistochemical staining of fixed tumor cell lines, as determined by intensity of nuclear staining, indicated increased expression of ANPG protein that correlated with the Northern blot data. Levels of ANPG message were also evaluated in 13 breast cancer tissues. Expression of ANPG message was increased 2-24 fold as compared with normal primary breast epithelial cells. These results indicated that ANPG expression is increased in breast cancer and that up-regulation of this gene may play a functional role in breast carcinogenesis.

Jennifer MacGregor
Ms. MacGregor was funded for a second year for her research on the estrogen receptor (see above).

Kristi Miller
Ms. Miller was funded for a second year for her research on p300 (see above).

Mairin Anderson
Optical imaging of breast tumors holds great promise of offering a safe, effective, noninvasive and inexpensive imaging modality. Optical contrast agents that absorb at the appropriate wavelength enhance and sharpen the images. Most importantly, compounds which localize in neoplastic tissue highlight the tumors. Earlier attempts to prepare such agents have focused on porphyrins, which accumulate in tumor tissue, but do not absorb adequately at the long wavelengths necessary for imaging. Ms. Anderson proposes to synthesize tetraazaporphyrins, a synthetically accessible type of porphyrinic macrocycle which has the optical characteristics necessary for imaging. Solubility and absorption spectra will be optimized by modifications to the periphery of the macrocycle to generate potential candidates for contrast agents in optical imaging of breast tumors.

Ken Geles
The transport of proteins and RNA across the nuclear envelope depends on the cooperation of both cytoplasmic and nuclear factors. The import of proteins through the nuclear pore complex requires three cytosolic factors: the nuclear localization sequence (NLS) receptor, p97 and Ran/TC4. Multiple NLS receptor homologues have been identified in mammalian cells. Analysis of NLS receptors in leukocyte and lymphocyte cell lines indicate that NLS receptor may play a role in carcinogenesis. Further support for NLS receptor's role in carcinogenesis has been obtained from BRCA1 subcellular localization experiments. BRCA1 can directly bind to the NLS receptor, but BRCA1 remains in the cytoplasm when transfected

into breast cancer cells despite identification of two functional NLS's. In contrast, BRCA1 accumulates in the nucleus of non-breast cancer cells, suggesting that there may be a defect in the nuclear import pathway of breast cancer cells. Mr. Geles has chosen the nematode C. elegans as a model to study the function and developmental regulation of NLS receptors in vivo.

Larissa Wenning, Ph.D.
Recent studies indicate that high-dose therapy in conjunction with peripheral blood stem cell transplantation results in higher response rates than conventional chemotherapy for treatment of metastatic breast cancer. The presence of tumor cells in the peripheral blood necessitates the use of purging techniques to eliminate the tumor cells prior to transplantation. However, the agents used to eliminate tumor cells also eliminate rapidly dividing hematopoietic progenitors, thus increasing the mortality due to delayed expansion of peripheral blood stem cells. One potential solution to this problem is the use of cytokine assisted ex vivo expansion of peripheral blood stem cells following purging to eliminate tumor cells. Dr. Wenning is studying the cytokine stem cell factor (SCF) to determine its effects on growth and differentiation of hematopoietic cells in stroma free culture. Mathematical modeling techniques will also be used to determine which hematopoietic processes are affected by SCF.

Program components
Dr. Jordan has established the Breast Cancer Journal Club to bring together the members of the Breast Cancer Training Program on a weekly basis to discuss relevant journal articles and areas of research. Training grant students participate and present at the journal club meetings. Students present a selected breast cancer topic from the basic and clinical literature and Dr. Jordan leads a discussion revolving around the topic. The journal club regularly attracts 10-15 graduate, postdoctoral and faculty participants in addition to the four predoctoral students and one postdoctoral fellow.

In addition to the Journal Club, Dr. Jordan also conducts a monthly breast cancer research meeting to bring together clinicians and basic scientists on both the Evanston and Chicago campuses of Northwestern. At the meetings faculty review progress on their research. Examples of research presented include: Jonathan Jones, Ph.D., Associate Professor, Cell and Molecular Biology, presented his research of the role of hemidesmosomes in breast cancer cells. Dr. Jones is testing whether loss of hemidesmosomes in breast cancers may enhance their ability to migrate and increase their proliferation. Ann Thor, M.D., Professor, Department of Pathology, Evanston Hospital, described her research on molecular markers in breast cancer. Dr. Thor is trying to correlate changes in markers with specific chemotherapy treatment regimens. One example of such a marker is Her B-2. William Lowe, M.D., Associate Professor, Medicine, presented his research on IL-1 signal transduction pathways in breast cancer cells. Dr. Lowe is generating IL-1 dominant negative growth factor receptors for these studies.

Students also attend numerous seminars and journal clubs throughout the year that have direct relevance to breast cancer. These include the Tumor Cell Biology Seminar Series, Cell

and Molecular Biology Seminars, Molecular Endocrinology Seminars and the newly established Translational Research Seminar Series. During the last two years the Lurie Cancer Center has sponsored the visit of several leading breast cancer research specialists, such as Kathryn Horwitz, Ph.D., Marc Lippman, M.D, Barry Gehm, Ph.D. and Marco Gottardis, Ph.D..

Publications

The success of the Lurie Cancer Center Breast Cancer Training Grant is exemplified by the numerous publications by the students as a direct result of their funding by the Molecular Biology of Breast Neoplasia Training Grant.

Student	# of Papers/Abstracts Submitted for Publication
S-J Teng	1
Sameer Mathur	1
Malathy Shanmugam	2
Julie McLachlan	1
Ann Buchmann	1
Stephanie Hsu	3
Todd McAdams	1
Zehan Chen, Ph.D.	3
Kristi Miller	0
Jennifer MacGregor	7
Jennifer Sanders	1
Sonia Cerda, Ph.D.	3

Publications

Buchmann A., Swaminathan S. and **Thimmapaya B**. Regulation of Cellular Genes in a Chromosomal Context by the Retinoblastoma Tumor Suppressor Protein. In Preparation.

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Shanmugam M, Krett N, Maizels ET, Rosen ST and **Hunzicker-Dunn M**. Acute Regulation of the Protein Kinase C Delta Isoform by PMA in MCF-7 and MDA-MB 231 Cells. The Endocrine Society 1996.

Conclusions

The Robert H. Lurie Cancer Center has established an outstanding program in breast cancer at Northwestern University. A critical component of this program is the US Department of Defense Training Grant "Molecular Biology of Breast Neoplasia". The training grant provides an exceptional environment to promote and advance the research potential of committed individuals. The program has enabled 12 predoctoral students and 3 postdoctoral fellows to be exposed to a solid foundation and knowledge base in breast cancer. The productivity of the students is significant as assessed by research publications. The program attracts a significant applicant pool each year. Students are selected based upon their academic credentials, letters of recommendation from their faculty sponsors, and the relevance of their research to breast cancer. The goal of the program is to train investigators to actively contribute to breast cancer related problems in their future research endeavors.

APPENDIX MATERIAL

Breast Cancer Program
Journal Club Schedule

September 9 - Gale England

September 16 - Ana Levinsen

September 23 - Kathy Yao

September 30 - Karin Klein

October 7 - Angela Cisneros

October 14 - Jennifer MacGregor

October 21 - Kristi Miller

October 28 - Ken Geles

November 4 - Mairin Anderson

November 11 - Rachel Duan

November 18 - JoAnne McAndrews

November 25 - Pei-Yu Chen

December 2 - San Antonio Meeting-no journal club

December 9 - Nancy Krett

December 16 - Hong Liu

December 23, 30 - Christmas/New Year Holiday

BREAST CANCER RESEARCH PROGRAM

All sessions will be held in the Vanderwicken Library, Olson Pavilion at 3:00 pm

Presentation Schedule

Monday, **April 8, 1996** 3:00 pm -	**Dr. Barry Gehm** "Site Directed Mutagenesis of estrogen Receptor
Monday **May 6, 1996**	**R. Chatterton** - "Development of hormone assays for epidemiological studies of premenopausal women"
Monday **June 10, 1996**	**Dr. Murthy** - Animals Models of Breast Cancer Metastases
Monday **July 8, 1996**	**Agostino Molteni** "Cytostatic properties of ACE Inhibitors" **Peter Gann** "Mitogenic Growth factors in nipple aspirates
Monday **August 5, 1996**	**Mimi Rodin** "Breast Cancer Screening among Indochinese immigrant women"
Monday **September 9, 1996**	**Jonathan Jones** (3-1412) "Hemidesmosomes and breast epithelial cells"
Monday **October 28, 1996**	**Ann Thor** Breast Cancer Research at Evanston Hospital
Monday **December 9, 1996**	**Bill Lowe** - Dominant negative growth factor receptors and breast cancer